

***Remarks***

Reconsideration of this Application is respectfully requested. Upon entry of the foregoing amendment, claims 63, 65, 66 and 71 are pending in the application, with claim 63 being the sole independent claim.

Claim 63 is sought to be amended without prejudice to or disclaimer of any deleted subject matter therein. Support for this amendment can be found in the specification, for example, at page 9, lines 28-31. Claim 68 is sought to be canceled without prejudice to or disclaimer of any deleted subject matter therein. Claim 71 is sought to be added. Support for claim 71 can be found in the specification, for example, in examples 1-8. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Enablement Rejections Under 35 U.S.C. § 112, First Paragraph***

Claims 63, 65 and 66 are rejected under 35 U.S.C. § 112, first paragraph for lack of enablement. Office Action, pages 2-8. Specifically, the Examiner states that the specification:

... does not reasonably provide enablement for an agent for treating pain, comprising a galactose-binding lectin, a L-chain or a L-chain fragment of a clostridial neurotoxin comprising the active proteolytic enzyme domain, and a translocation domain of a clostridial neurotoxin H-chain, wherein the lectin, L-chain or L-chain fragment, and the translocation domain are linked together by a covalent bond, and wherein the lectin is of bacterial origin, or the lectin has been treated with a modifying chemical and

retains an ability to bind an oligosaccharide structure having an exposed galactose or N-acetylgalactosamine residue.

*Id.* at page 3, lines 5-12.

Applicants respectfully traverse the rejection. However, solely to expedite prosecution and not in acquiescence to the rejection, Applicants have removed those portions of claims which are alleged by the Examiner to lack enablement. Accordingly, it is believed that the enablement rejection under 35 U.S.C. §112, first paragraph has been rendered moot.

Moreover, to facilitate its allowance, Applicants have amended claim 63 as proposed by the Examiner<sup>1</sup> with the following exception: instead of reciting in the last clause that "the LH<sub>N</sub> and the lectin are linked by SPDP," Applicants' amended claim 63 recites that "the LH<sub>N</sub> and the lectin are linked together by contacting the LH<sub>N</sub> and the lectin with one or more chemical coupling agents." Support for this amendment can be found in the specification, for example, at page 9, lines 28-31.

Further to 37 C.F.R. § 1.132, Applicants also submit herewith declarations by Dr. John Chaddock and Dr. Keith Foster. These declarations and their accompanying annexes demonstrate that the skilled artisan, at the time the application was filed, would know how to make and use the claimed invention without undue experimentation. In particular, the declarations refer to pre-1997 publications describing commercially available coupling agents which the skilled artisan would know how to use to link proteins or protein derivatives. The declarations also refer to publications demonstrating that the skilled artisan would know how to confirm L-chain, H-chain and targeting

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<sup>1</sup> The Examiner's proposed amendment is part of an Interview Summary attached to the Office Action.

moiety function after chemical coupling. Hence, these declarations provide additional evidence that the claims are enabled.

It is respectfully requested that the enablement rejection be withdrawn and that the claims be allowed.

***Written Description Rejections Under 35 U.S.C. § 112, First Paragraph***

Claims 63, 65 and 66 are also rejected under 35 U.S.C. § 112, first paragraph for lack of an adequate written description. Office Action, page 8-9. Specifically, the Examiner states that the specification:

... does not describe the preparation of the conjugate of the lectin directly linked to an L chain or an HN domain of a clostridial toxin, and the fusion protein of galactose-binding lectin, an L-chain of a clostridial neurotoxin, and a translocation domain of a clostridial neurotoxin H-chain without a proper spacer, nor indicates the treatment of a galactose-binding lectin with a modifying chemical, e.g., what modifying chemical is used, and what effect the modified lectin has in respect to the binding to a galactose or an N-acetylgalactosamine residue.

Office Action, page 9, lines 4-10.

Applicants respectfully traverse the rejection. However, solely to expedite prosecution and not in acquiescence to the rejection, Applicants have removed those portions of claims which are alleged by the Examiner to lack adequate written description. Accordingly, it is believed that the written description rejection under 35 U.S.C. §112, first paragraph has been rendered moot.

As described above, Applicants' amended claim 63 recites that "the LH<sub>N</sub> and the lectin are linked together by contacting the LH<sub>N</sub> and the lectin with one or more chemical coupling agents." Adequate written description support for this amendment can be found, for example, in the specification which states that "in one embodiment of the

invention a galactose-binding lectin is conjugated, using linkages that may include one or more spacer regions, to a derivative of the clostridial neurotoxin." Page 9, lines 28-31. As noted by the Examiner, the specification provides examples using an SPDP linker. Office Action, page 9, line 1-4. Furthermore, the specification refers to WO96/33273 which describes clostridial neurotoxin derivatives conjugated to targeting moieties using PDPH/EDAC, or Traut's reagent. Specification, page 8, lines 5-15; and page 9, lines 16-27. *See also* Declarations, page 2, first full paragraph, provided herewith. Moreover, this published international application explicitly indicates that "any other coupling chemistry . . . known to those of skill in the art" could be used. *Id.* As described above, the Declarations submitted herewith also refer to pre-1997 publications demonstrating that the skilled artisan, at the time the application was filed, recognized a class of well known coupling agents for linking proteins.

Hence, the skilled artisan upon reading Applicants' specification would recognize that there is a well known class of chemical coupling agents that can be used to link the LH<sub>N</sub> and the lectin. Thus, the skilled artisan would recognize that Applicants were in possession of the invention as claimed at the time the application was filed. Therefore, Applicants' specification provides an adequate written description of the invention as claimed.

It is respectfully requested that the written description rejection be withdrawn and that the claims be allowed.

***Rejections under 35 U.S.C. § 112, second paragraph***

Claims 63, 65 and 66 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as their invention. Office Action, page 10, paragraph 6.

Applicants respectfully traverse the rejection. However, solely to expedite prosecution and not in acquiescence to the rejection, Applicants have removed those portions of claims which are alleged by the Examiner to be indefinite. Accordingly, it is believed that the indefiniteness rejection under 35 U.S.C. §112, second paragraph has been rendered moot. Hence, it is respectfully requested that this rejection be withdrawn and that the claims be allowed.

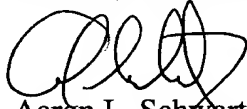
***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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